

Workshop on priorities for epidemiologic studies on occupational cancer

A large number of epidemiologic studies investigating cancer risk in industrial populations are published every year in the scientific literature. A rather large proportion is concerned, however, with further investigation of already established risks, and the few new studies are inadequate to address the growing number of exposures with sufficient evidence of carcinogenicity in animals for which epidemiologic data from humans are lacking. Other potentially important observations such as case reports and associations found by linkage of exposure data and routine vital statistics are not always being followed-up.

These considerations prompted the International Agency for Research on Cancer (IARC), in collaboration with the Commission of the European Communities (CEC), to convene a meeting of a group of epidemiologists and industrial hygienists active in the field of occupational cancer in Europe and North America. The purpose of the meeting was (i) to exchange information on the current pattern of epidemiologic research on occupationally related cancer, (ii) to develop possible criteria for setting priorities for research in occupational cancer epidemiology, and (iii) to examine the feasibility of preparing a list of occupations or occupational exposures which should be considered by those planning epidemiologic studies.

The overriding purpose was to encourage research in areas which will have the maximum occupational and public health impact by preventing avoidable cancers. On the basis of the experience of investigators from the countries represented at the meeting, we have compiled a list of ten criteria to help in selecting occupational exposures for epidemiologic study.

Description of the ten criteria

1. Number of workers exposed.

Clearly, if the agent proves deleterious to humans, the number of workers adversely affected would be directly related to the number of workers exposed. Various data bases are available that may be used to estimate the exposed number. Many of these data bases derive from broad surveys or samples of industry. Therefore, care must be exercised since they may inaccurately reflect the actual number of workers exposed. In addition extrapolating from the samples of industry to the number of exposed workers is correct only when the sampling design was intended to estimate the proportion of exposed to some specific chemical.

2. Level of exposure of workers.

The fact that a chemical may be commonplace in industry does not necessarily mean that exposure is substantial. The level of exposure of workers to the chemical of interest should be used as a criterion for prioritization. These data are often limited. It may be necessary to conduct surveys of the characteristics of exposure in industry to gather appropriate information.

3. Quality of exposure data.

The validity of the results depends on the quality of the information available on exposures. For the investigation of a dose-response relationship, estimates of individual exposure are needed. The more reliable the estimate, the greater the priority for a study.

4. Carcinogenic potential.

Evidence that an agent is a carcinogen in experimental studies should raise the level of priority for study. Current IARC monographs rate agents as to whether there is sufficient experimental evidence of carcinogenicity. In the future, quantitative ratings of toxicity may prove useful in the effort to prioritize chemicals for study. Experimental evidence of clastogenicity, mutagenicity and structure-function relationships, alkylation of DNA (deoxyribonucleic acid), generation of free radicals, etc, should also be considered.

5. Evidence of human carcinogenicity.

Case reports or preliminary epidemiologic studies that do not settle the issue should enhance the priority of a study. Human evidence of clastogenicity and mutagenicity should be considered positively.

Sufficient evidence of human carcinogenicity should generally dissuade researchers from further study. Not only is there no need to reconfirm sound evidence of carcinogenicity, but such efforts take resources from other studies. While studies on established carcinogens (eg, asbestos, radiation, etc) may be worth conducting to investigate dose-response relationships, mechanisms of action, etc, such a class of studies should definitely have a lower priority than studies aimed at ascertaining the presence or absence of a new hazard. Mere replication of studies that may add to the scientific literature but not to the body of scientific understanding should be discouraged.

6. Ongoing exposure to known carcinogens at permissible levels of exposure.

The exception to the criterion that valid positive studies do not need repetition would be the study of a known carcinogen at reduced, permissible levels of exposure. Regulatory history demonstrates that exposure to numerous occupational hazards has been permitted at ever reducing levels (eg, asbestos, 2-naphthylamine).

7. Trends in exposure.

Suspect carcinogens the use of which is on the rise and is therefore leading to increased potential exposure of workers should receive a higher priority for study than agents whose use is stable or waning.

Particular attention should be given to trends of production and import in countries of recent industrialization where little epidemiologic research is being carried out. Given the less stringent regulation in the currently industrializing countries, the potential for hazardous exposure is likely to be increasing in those countries.

8. Control of confounding factors.

A major component of the validity of a study, and hence important in determining if a study is feasible, is the identification and evaluation of confounding factors, both occupational and nonoccupational, in the study population. Suspect carcinogens that can be studied with control of confounding factors should receive a higher score. For example, studies of a suspect lung carcinogen should receive a higher priority ranking if relevant data on smoking are available or can be assembled.

9. Cases potentially attributable to exposure.

The number of cases of cancers potentially attributable to exposure is a function of the carcinogenicity of the agent, level of exposure, number of workers exposed, etc. In epidemiologic terms, the number of attributable cases is a function of the rate of disease in the population, relative risk in the study population, and size of the exposed population. Occupational exposures that will potentially result in a greater number of attributable cases should receive a higher score on this criterion.

On occasion there may be exposure (at levels lower than at the workplace) for residents of the community to an agent that is not currently a health concern in

the workplace. Although the risk may be quite low, the large number of potentially exposed persons may suggest the usefulness of studies of occupational exposures, the results of which might be extrapolated to lower environmental exposure situations.

10. Time since first exposure.

Several years are usually required for a malignant disease to become apparent after the first exposure to a carcinogen. Therefore priority should be given to studies of populations for which sufficient time has elapsed since first exposure.

The Working Group has decided to verify the applicability of the preceding criteria in different national situations and thereby to develop a list of priority research areas. We recognize that these criteria may not be optimal, and we encourage researchers in the field to use them and report to us modifications that would enhance their usefulness.

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